



Case Report

Serial measurement of glyphosate blood concentration in a glyphosate potassium herbicide-intoxicated patient: A case report



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ABSTRACT

Introduction: This report describes changes in blood and urine concentrations of glyphosate potassium over time and their correlations with clinical symptoms in a patient with acute glyphosate potassium poisoning.

Case report: A 67-year-old man visited the emergency center after ingesting 250 mL of a glyphosate potassium-based herbicide 5 h before. He was alert but presented with nausea, vomiting, and bradyarrhythmia with atrial fibrillation (tall T waves). Laboratory findings revealed a serum potassium level of 6.52 mEq/L. After treatment with an injection of calcium gluconate, insulin with glucose, bicarbonate, and an enema with polystyrene sulfonate, the patient's serum potassium level normalized and the bradyarrhythmia converted to a normal sinus rhythm. During admission, the blood and urine concentration of glyphosate and urine aminomethylphosphonic acid (AMPA, a glyphosate metabolite) was measured at regular time intervals. The patient's glyphosate blood concentration on admission was 11.48 mg/L, and it had decreased rapidly by 16 h and maintained about 1 mg/L by 70 h after admission. Urine glyphosate and AMPA levels had also decreased rapidly by 6 h after admission.

Discussion: Glyphosate potassium poisoning causes hyperkalemia. Blood concentrations of glyphosate were decreased rapidly by 16 h after admission, and urine concentrations were also decreased by 6 h after admission.

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1. Introduction

Glyphosate potassium is one of glyphosate's derivatives that enhances absorption and delivery to the leaf surface. We describe here changes in blood and urine concentrations of glyphosate and potassium over time in a patient with acute glyphosate potassium poisoning.

2. Case report

A 67-year-old male patient presented to an emergency department with chief complaints of abdominal discomfort, nausea, and vomiting. He had drunk 250 mL of an herbicide called Touchdown IQ® (glyphosate potassium, 44.75%; surfactant, adjuvant, antifoaming agent, bulking agent, 55.25%; Syngenta Korea Corp.) during a suicide attempt 5 h earlier. At the time of the visit, his blood pressure was 110/60 mmHg, heart rate was 67 beats/min, breathing rate was 20 breaths/min, body temperature was 36.9 °C and the patient was fully conscious. No unique

findings were made during the physical examination other than mild tenderness in the upper abdomen. He has no specific medical history including kidney disease. Results of the arterial blood test performed immediately after the visit showed that he had metabolic acidosis and hypoxemia (pH, 7.28; pCO₂ level, 27 mmHg; pO₂ level, 66 mmHg; HCO₃ level, 12.7 mmHg; O₂ saturation, 90%; anion gap, 14.4; and lactic acid, 4.3 mmol/L); as a result, we administered 3 L/min of O₂ through a nasal cannula to the patient. In the electrolyte examination, the Na⁺ level was 138.8 mEq/L, K⁺ level was 6.52 mEq/L, and Cl⁻ level was 111.7 mEq/L, indicating that the patient had hyperkalemia. Results of the biochemical examination showed that his blood urea nitrogen level was 21.0 mg/dL and creatinine level was 1.27 mg/dL.

While waiting for the blood test results, the patient's heart rate decreased to 52 beats/min; showing atrial fibrillation with tall T waves. After confirming hyperkalemia, calcium gluconate (2 g), regular insulin (10 IU), and sodium bicarbonate (40 mEq) were administered intravenously, and an enema was administered three times using polystyrene sulfonate (30 g) to remove the potassium from the body. Four hours after the visit, the patient's heart rate has increased to 66 beats/min with showing normal sinus rhythm. Results of the arterial blood test at that time were as follows: pH, 7.42; pCO₂ level, 29 mmHg; pO₂

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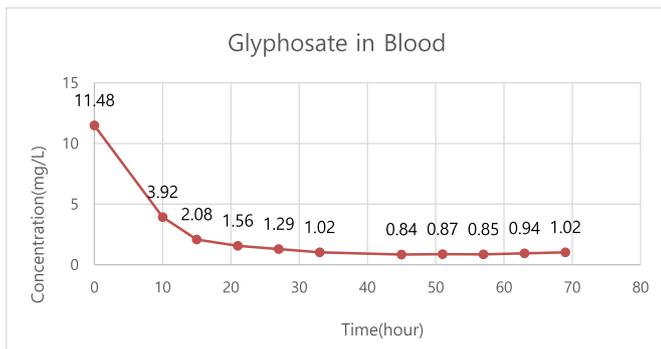


Fig. 1. Blood glyphosate levels by regular time intervals.

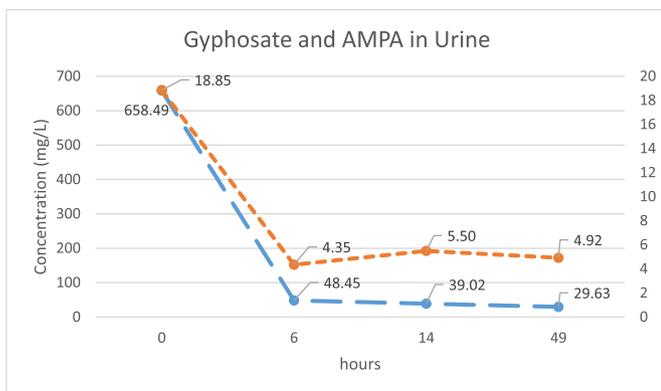


Fig. 2. Urine levels of glyphosate and AMPA (aminomethylphosphonic acid) by regular time intervals.

level, 94 mmHg; HCO_3^- level, 18.8 mmHg; and O_2 saturation, 97%. In the electrolyte examination, the levels of electrolytes were as follows: Na^+ , 139.6 mEq/L; K^+ , 5.60 mEq/L; and Cl^- , 112.2 mEq/L.

The patient was hospitalized for further monitoring. After 3 days of monitoring, he was discharged, as no additional abnormal findings were made and his symptoms had improved. After receiving informed consent, serial blood and urine samples were collected during his hospital stay and sent to the National Forensic Service of Korea to analyze the concentration of toxic materials. Figs. 1 and 2 show the changes in blood and urine concentrations of glyphosate and its metabolite, aminomethylphosphonic acid (AMPA) over time. The glyphosate blood concentration at admission was 11.48 mg/L, and it decreased rapidly by 16 h. Urine glyphosate and AMPA concentrations were also decreased rapidly by 6 h after admission.

3. Discussion

Human metabolism of glyphosate was not yet known, as it had previously been studied only in animals. Han et al. reported the results of an analysis of blood concentrations of 5 patients who ingested glyphosate. In that study, they analyzed blood concentration at admission time, not serially. They reported that blood concentrations at admission varied from 1.0 to 171.1 $\mu\text{g/mL}$ (0.01–1.71 mg/L) depending on the ingested amount [1]. In a recent Japanese study, the main cause of death from glyphosate potassium poisoning was cardiac toxicity due to hyperkalemia [2]. Based on that study, we assumed that hyperkalemia in our patient was induced by the ingestion of exogenous potassium accompanied by glyphosate intoxication.

In an animal study [3], the maximal plasma concentration time of glyphosate was 5.16 h. The half-life of oral absorption was 2.29 h, and the elimination half-life was 14.38 h. Since the current patient visited a hospital 5 h after being poisoned, it can be assumed that most of the ingested glyphosate was absorbed. Most of ingested glyphosate is excreted through urine and feces within 72 h in rat study [4]. In our patient, the blood concentrations of glyphosate drastically decreased within 16 h after ingestion and maintained about 1 mg/L by 70 h, and the urine concentrations of glyphosate and AMPA decreased within 6 h, although no special treatment were taken to decrease the level. Although we assume that the metabolism of glyphosate in human did not greatly differ from that in animals, we could not find any studies that continuously measured the levels of glyphosate in humans. As far as we know, this case report is the first to describe blood and urine concentrations of glyphosate at regular time intervals in a patient hospitalized due to glyphosate potassium poisoning.

Disclosure

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

References

- [1] Han J, Moon H, Hong Y, et al. Determination of glyphosate and its metabolite in emergency room in Korea. *Forensic Sci Int* 2016;265:41–6.
- [2] Kamijo Y, Takai M, Sakamoto T. A multicenter retrospective survey of poisoning after ingestion of herbicides containing glyphosate potassium salt or other glyphosate salts in Japan. *Clin Toxicol (Phila)* 2016;54:147–51.
- [3] Anadón A, Martínez-Larrañaga MR, Martínez MA, et al. Toxicokinetics of glyphosate and its metabolite aminomethyl phosphonic acid in rats. *Toxicol Lett* 2009;190:91–5.
- [4] Williams GM, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. *Regul Toxicol Pharmacol* 2000;31:117–65.